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Evaluation of Long-Term Complications of Diabetes Mellitus in Dogs.

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ABSTRACT

Diabetes mellitus (DM) is indeed considered a metabolic disease-causing chronic complication in several organs. The present study aimed to investigate long-term complications in diabetic dogs. This study was performed on 50 chronically diabetic dogs (aged 6–14 years) compared to 20 healthy control dogs. Clinically, affected dogs showed polydipsia, polyuria, polyphagia, eye cataracts, and emaciation. There was a highly significant decrease in Total erythrocytic count, hemoglobin, packed cell volume, and lymphocyte levels; however, there was a significant increase in white blood cells, neutrophils, and platelet levels in diabetic dogs. Biochemically, diabetic dogs showed a significant increase in random blood glucose, hemoglobin A1C (HbA1C), kidney markers Symmetric dimethylarginine (SDMA), cardiac markers (Troponin T and creatine kinase-myocardial band (CK-MB)), and a significant decrease in immunoglobulins (IgG, IgM, and IgA). Electrocardiographic examination showed abnormal T-waves (wide and enlarged) and cardiac arrhythmia. Ultrasonographic and radiographic examinations showed pancreatitis, fatty liver, nephritis and emphysematous cystitis. In conclusion, this study revealed that diabetes mellitus in dogs resulted in multiple complications. Therefore, it is recommended to monitor and manage chronically diabetic dogs to control these complications.

1. INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia that results from insulin secretion deficiencies, insulin resistance, or both. Diabetes-related chronic hyperglycemia has been associated with long-term organ damage, problems, and failure (American Diabetes Association, 2013). DM is a major cause of morbidity and mortality and a substantial risk factor for the quick onset of coronary heart disease (Bailes 2002). Hyperglycemia interferes with glucose, lipid, protein, and electrolyte metabolism; each of these can have an effect on the blood vessels and endothelial capillaries, which are found in the retina, kidney, and nerves. These conditions are related to excessive and dangerous glucose accumulation in these cells (Lotfy et al., 2017). Diabetic retinopathy is one of the most prevalent diabetic complications, affecting the small blood vessels in the retina of the eye. Several factors influence the development of diabetic retinopathy, including the duration and severity of hyperglycemia and other underlying health conditions such as hypertension (Garca-Ocaa et al., 2020). Cataracts in the eyes are considered to be prevalent and serious consequences of diabetes. (Wilkie et al. 2006). Diabetes mellitus is linked to a number of liver problems, such as unusual glycogen deposition, fibrosis, cirrhosis, hepatocellular carcinomas, chronically high levels of hepatic enzymes, acute liver diseases, and hyperglycemia, which damages hepatocytes (Mohamed, 2016). Diabetes is the most prevalent cause of chronic kidney disease (CKD), and anemia is a common complication among patients with both diabetes and CKD. Low hemoglobin levels in patients with diabetes and CKD have been linked to an increased risk of kidney disease progression, cardiovascular morbidity, and mortality (Mehdi and Toto 2009). Symmetric dimethylarginine (SDMA) is a novel renal biomarker that properly depicts the rate of glomerular filtration in contrast with serum creatinine. SDMA is a catabolic byproduct that is primarily eliminated by the kidneys. SDMA levels increase earlier in the course of kidney disease, with just a 25 to 40% drop in Glomerular filtration rate (GFR) leading to an increase in SDMA, whereas creatinine levels will not rise until GFR falls by 75%. This means that SDMA can enable earlier diagnosis of kidney dysfunction (Elgazzar et al. 2022). Cardiovascular disease (CVD) is a major cause of mortality in patients with both type 1 and type 2 diabetes. Numerous factors, such as hypertension, obesity, and dyslipidemia, affect the risk of CVD. Coronary heart disease (CHD) is one of the most common macrovascular complications associated with diabetes. There is a higher risk of developing CHD due to several factors, including insulin resistance, inflammation, and abnormal lipid metabolism. In diabetic patients, chronic hyperglycemia also contributes to the development and progression of CHD and increases the possibility of myocardial infarction (Garca-Ocaaet et al., 2020). Therefore, the current study was designed for the evaluation of long-term complications of diabetes mellitus affecting different organs, including the eye, liver, kidney, and heart, in dogs.

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2. MATERIAL AND METHODS

2.1 Animals

The current study was applied to 50 diabetic dogs compared to 20 healthy control dogs different in age (6–14 years), sexes (30 males and 40 female), weight (5–45 kg), and breeds (German shepherd, Golden retriever, Black Rottweiler, Pitbull, Mastiff, Pekingese, and Husky) with a history of DM for more than 2 years. The dog's clinical cases belonged to private pet animal clinics and shelters located in Cairo and Kalioubia governorates in the period from July 2022 to July 2023. The dogs were diagnosed to be affected with DM based on clinical and hemato-biochemical examinations, urinalysis, ultrasonography examinations, X-ray and electrocardiographic examinations. The positive cases of DM were confirmed by an RBG of >180 mg/dl and an HbA_{1C} of more than 6%.

2.2. Ethical approval

All examinations were done after the approval of the Ethics committee of Benha University with the approval number: BUFVTM05-02-23

2.3. Urine examination

Urine samples were collected using sterile urethral catheterization, and urinalysis was performed with commercial urine strips (COMBI-9 strips provided by Pasteur Lab. in Egypt). to determine the presence of glucose, specific gravity, protein, PH, WBCs, and others (Choudhary et al., 2021).

2.4. Hematological analysis

Total erythrocytic count (RBCs), hemoglobin concentration (Hb), packed cell volume (PCV), total leukocytic count (WBCs), and differential leukocytic counts, platelets were determined by a hematological analyzer (Biotec Hema 21) on freshly collected blood samples with anticoagulant.

2.5. Biochemical analysis

The obtained serum samples were used for the spectrophotometric determination of serum concentrations of random blood glucose, BUN, creatinine, AST, ALT, IgG, IgM, IgA, Troponin T, and CK-MB by using commercial kits of the spectrum (Egyptian Company for Biotechnology (S.A.E.), Obour City Industrial Area, Cairo, Egypt). SDMA was estimated by commercial kits (IDEXX Laboratories). HbA_{1c} was determined by the SCA 1000 analyzer on freshly collected blood samples with anticoagulant.

2.6. Electrocardiographic examinations

ECG traces in small animals were recorded on a bipolar base apex lead system using lead II and an ECG monitor, according to Martin (2015). ECG waves were recorded with a single-channel electrocardiographic machine (BTL-08 SD ECG, Industries Ltd., 161 Cleveland Way, Stevenage, SG1 6BU U.K.) with a paper speed of 25 mm/s and a calibration of 10 mm equal to 1 mV. The amplitudes and durations of all waveforms were calculated manually, where each small square represents 0.02 ms on the vertical plane and 0.1 mv on the horizontal plane.

2.7. Ultrasonography and radiographic examinations

An ultrasonography examination was performed on the pancreas, liver, and kidney. The dogs were controlled in lateral recumbency during the ultrasonographic examination, which was performed without sedation or anesthesia. The pancreas is usually examined by a ventral abdominal approach. A right intercostal approach was occasionally utilized in deep-chested dogs to examine the right lobe. Within 24 to 48 hours following the test, a written report was generated (Bolton et al., 2016). Right lateral recumbency was employed for right kidney examinations, while left lateral recumbency was applied for left kidney examinations. The left and right kidneys were examined under the transverse processes of the first and third lumbar vertebrae. Chison E2 portable ultrasound with a 5-8 microconvex transducer was used to detect any changes in tissue architecture and kidney size (Elgazzar et al., 2022). The transducer was positioned caudal to the animal's xiphoid, and the beam of ultrasound was directed cranially. The image that resulted showed the liver and the gallbladder in a longitudinal view, with the diaphragm apparent as an echogenic cranial boundary (Mwanza *et al.*, 1998). Conventional abdominal radiography was carried out by a HP X ray machine (Italy). Lateral radiography of the dog's abdomen was performed according to Fabbi et al. (2016).

2.8. Statistical analysis

The statistical analysis was carried out using T-test and correlation using SPSS, ver. 25 (IBM Corp. Released 2013). Data were handled with a complete randomization design, according to Steel et al. (1997). Multiple comparisons were carried out applying Duncun test the significance level was set at $P < 0.05$. Person-to-person correlation was performed between RBG, HbA1C, and other markers according to ver. 27 (IBM Corp. Released 2013).

3. RESULTS

Clinical Findings

Chronically diabetic dogs suffer from retinal degeneration, nephropathy, hepatopathy, and heart disease. Besides, the symptoms of diabetes include polyuria, polydipsia, polyphagia, emaciation, pale mucous membrane, and eye cataract (Fig. 1). The physical examination revealed an increased pulse rate (100–160 pulses/minute) with normal temperature and respiration.

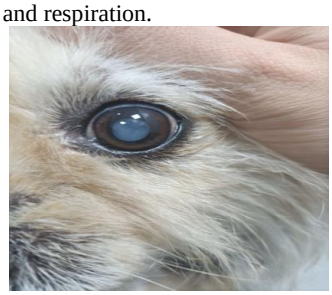

Figure 1 Eye cataract in diabetic Pekingese dog

Urinalysis

Urinalysis of diabetic dogs revealed highly significant glucosuria, a significant increase in specific gravity with highly acidic pH, the presence of leukocytes in their urine and proteinuria (Table 1).

Table 1 Changes in urinalysis in diabetic and control dogs.

Parameters	Control (N=20)	Diabetic (N=50)
Glucose	-	+++
Protein	-	++
pH	6	5
Leukocytes	-	+++
Nitrite	-	+
S. G	1.015	1.030

S. G: specific gravity

Hematological findings

There was a highly significant decrease ($P < 0.05$) in RBCs, Hb, PCV, and lymphocyte levels; however, there was a

significant increase in WBCs, neutrophils, and platelet levels in diabetic dogs compared to control dogs (Table 2).

Table 2 Hematological changes in diabetic and control dogs.

Parameters	Group		P-value
	Control (N=20)	Diabetic (N=50)	
RBCs ($x10^9/mm^3$)	6.52±0.69	3.97±0.23**	0.001
Hb (g/dL)	11.70±0.10	8.68±0.65*	0.029
PCV (%)	32.83±0.85	17.92±0.53***	0.000
WBCs ($x10^3/mm^3$)	12.83±0.44	25.77±2.18*	0.020
Neutrophil (%)	62.33±6.69	76.09±2.36*	0.036
Lymphocyte (%)	44.87±5.67	15.75±1.78***	0.000
PLT ($x10^3/mm^3$)	140.33±20.5	222.83±14.62*	0.021

PLT: platelets
Data are demonstrated as (mean ±SE)
Non-Significant :* Significant **: High significant
***: Very high significant.

Biochemical parameters

Diabetic dogs showed a significant increase ($P < 0.05$) in RBG compared to control dogs (Table 3). Diabetic dogs showed a significant increase in HbA_{1C} compared to control dogs (Table 3). Diabetic dogs showed a significant increase ($P < 0.05$) in AST, and ALT levels compared to control dogs (Table 3). Diabetic dogs showed a significant increase ($P < 0.05$) in BUN and Cr levels compared to control dogs (Table 3). Diabetic dogs showed a significant increase ($P < 0.05$) in SDMA levels compared to healthy control dogs (Table 3). Diabetic dogs showed a significant decrease ($P < 0.05$) in serum IgG, IgM, and IgA levels compared to control dogs (Table 4). Diabetic dogs showed a significant increase ($P < 0.05$) in Troponin T, CK-MB levels compared to control dogs (Table 4).

Table 3 Changes in blood glucose levels and liver and kidney function in diabetic and control dogs.

Parameters	Group		P-value
	Control (N=20)	Diabetic (N=50)	
RBG (mg/dL)	92.40±7.58	355.39±7.34***	0.000
AST (U/L)	25.98±3.88	56.67±4.22**	0.009
ALT (U/L)	30.95±2.42	159.21±5.57**	0.004
BUN (mg/dL)	20.89±4.95	74.51±6.00**	0.002
Cr (mg/dL)	0.88±0.06	3.88±0.47*	0.025
HbA_{1C} (%)	4.20±0.26	12.03±2.04*	0.028
SDMA (µg/dL)	11.60±0.51	32.67±6.53*	0.017

RBG; random blood glucose., AST; aspartate aminotransferase ALT; Alanine transaminase., BUN; blood urea nitrogen., Cr; creatinine., HbA1C; Hemoglobin A_{1C}., SDMA; Symmetric dimethylarginine .
Data are demonstrated as (mean ± SE): Non-Significant :* Significant
: High significant *: Very high significant.

Table 4 Changes in immunoglobulin (IGG, IGM, IGA) and cardiac markers in diabetic and control dogs.

Parameters	Group		P-value
	Control (N=20)	Diabetic (N=50)	
IgG (mg/dL)	690.67±5.81	416.00±7.57**	0.005
IgM (mg/dL)	217.32±3.93	192.05±3.65**	0.009
IgA (mg/dL)	42.20±2.97	18.01±4.64*	0.012
CK-MB (U/dL)	51.80±5.67	338.52±8.39***	0.000
Troponin T (ng/mL)	0.04±0.01	3.00±0.03***	0.000

CK-MB cardiac markers; creatine kinase-myocardial band
Data are demonstrated as (mean ± SE): Non-Significant :* Significant
: High significant *: Very high significant.

Electrocardiographic findings

The diabetic dogs suffered from abnormal T-waves (wide and enlarged) (Fig 2) and may be more prone to developing arrhythmia (Fig 3), such as ventricular tachycardia or fibrillation, which can result in the absence of a QRS wave on the ECG.

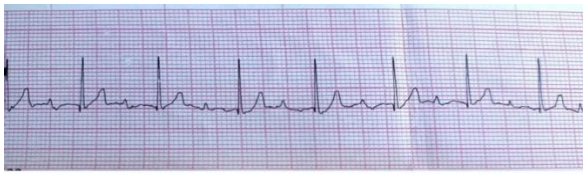

Figure 2 abnormal T-waves (wide and enlarged) in diabetic dog

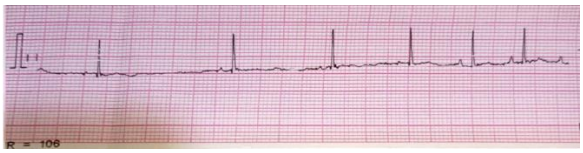

Figure 3 cardiac arrhythmia in diabetic dog

Ultrasonographic and radiographic findings

In Diabetic dogs suffering from pancreatitis, the pancreas may become more heterogeneous in texture, with areas of hypoechoic (darker) and hyperechoic (brighter) regions due to necrosis and hemorrhage. The pancreatic duct may also become dilated, and there may be surrounding fluid accumulation or inflammation in the adjacent tissues (Fig 4). Diabetic dogs suffer from fatty liver or hepatic lipidosis, and the echogenicity of a fatty liver on ultrasound is typically increased, meaning that it appears brighter or more hyperechoic than normal liver tissue and increases in liver size, also known as hepatomegaly (Fig 5). Ultrasonography of the kidneys revealed nephritis, increased echogenicity of the renal cortex, which appears brighter or more hyperechoic than usual on ultrasound. The kidneys may also appear smaller in size due to scarring or loss of functioning renal tissue (Fig. 6). Radiography of diabetic dogs showed emphysematous cystitis, and gas within the bladder lumen was easily detected (arrowheads) (Fig 7).

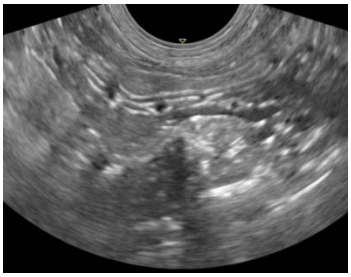

Figure 4 The pancreas of diabetic dog become more heterogeneous in texture, with areas of hypoechoic (darker) and hyperechoic (brighter) regions due to necrosis and hemorrhage. The pancreatic duct may also become dilated, and there may be surrounding fluid accumulation or inflammation in the adjacent tissues

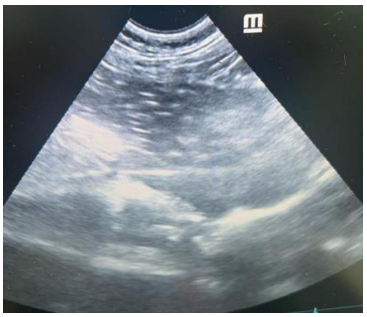

Figure 5 Liver of a diabetic dog, the echogenicity of a fatty liver on ultrasound is typically increased, meaning that it appears brighter or more hyperechoic than normal liver tissue and increase in liver size

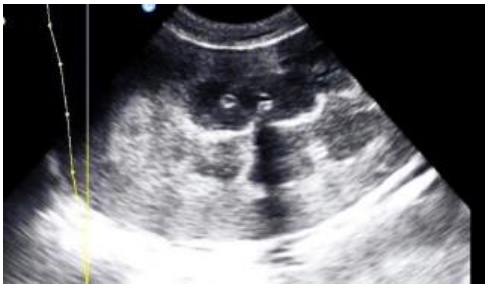

Figure 6 Kidney of diabetic dogs showed changes including increased renal cortex echogenicity, which appears brighter or more hyperechoic

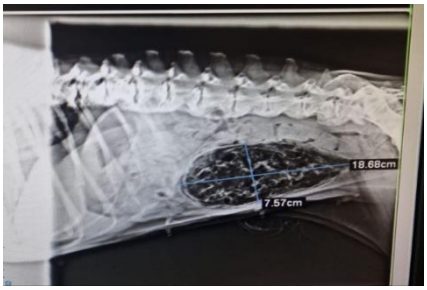

Figure 7 Urinary bladder of diabetic dog showed emphysematous cystitis and gas within the bladder lumen was easily detected (arrowheads)

Pearson Correlation between different parameters

Our findings revealed a significant positive correlation (P<0.05) between blood glucose levels (RBG, HbA1c) and hepatic function (Table 5). Our results showed a significant positive correlation (P<0.05) between blood glucose level (RBG, HbA_{1c}) and kidney functions (Table 5). However, a significant negative correlation (P<0.05) between cardiac damage markers (Troponin T, CK-MB) and immunoglobulins was demonstrated (IgG, IgM, IgA) (Table 6). Our results showed a significant positive correlation ($P < 0.05$) between blood glucose level (RBG, HbA_{1c}) and cardiac damage markers (Troponin T and CK-MB) with a significant negative correlation with immunoglobulins (IgG, IgM, IgA) (Table 6).

Table 5 Pearson Correlation between blood glucose level (RBG, HbA1C) and liver and kidney function in diabetic dogs.

	AST	ALT	BUN	Cr	HbA_{1C}	SDMA
RBG	0.180	0.201	0.088	0.116	0.340	0.623*
	0.260	0.207	0.585	0.470	0.182	0.040
AST		0.167	0.226	0.310*	0.500*	0.766*
		0.296	0.155	0.048	0.041	0.006
ALT			0.079	0.061	0.294	0.582
			0.622	0.703	0.252	0.061
BUN				0.590***	0.538*	0.646*
				0.000	0.026	0.032
Cr					0.802***	0.492
					0.000	0.124
HbA_{1C}						0.781**
						0.005

The direct correlation is represented by a positive sign.
The indirect correlation is represented by a negative sign.

Table 6 Pearson Correlation between blood glucose level (RBG, HbA1C) and immunoglobulin parameters and cardiac markers in diabetic dogs.

		Troponin T	IGG	IGM	IGA	RBG	HbA_{1C}
CKMB	Pearson Correlation	.998**	-.962**	-0.75	-.919**	.971**	.877*
	Sig. (2-tailed)	0.00	0.00	0.09	0.01	0.001	0.022
Troponin T	Pearson Correlation		-.951**	-0.72	-.916*	.973**	.868*
	Sig. (2-tailed)		0.00	0.11	0.01	0.001	0.025
IGG	Pearson Correlation			.898*	.949**	-.885*	-.953**
	Sig. (2-tailed)			.015	.004	0.019	0.003
IGM	Pearson Correlation				.837*	-0.599	-.930**
	Sig. (2-tailed)				.037	0.209	0.007
IGA	Pearson Correlation					-.822*	-.936**
	Sig. (2-tailed)					0.045	0.006

The direct correlation is represented by a positive sign.
The indirect correlation is represented by a negative sign.

4. DISCUSSION

Diabetes mellitus is considered a metabolic disease resulting in prolonged hyperglycemia that causes multiple complications in diabetic dogs (Arya et al., 2011). The diabetic dog suffers from polyuria, polydipsia, and polyphagia because of impaired blood glucose uptake by the liver, muscle, and adipose tissues and unregulated glucose synthesis in the liver, resulting in hyperglycemia, as reported by Bruyette et al. (2020). Almost the majority of the blood glucose is passively filtered into the ultrafiltrate by the glomerulus of the kidney. Only a fixed amount of glucose from the ultrafiltrate can be reabsorbed by the kidney's proximal tubule receptors. The renal threshold is a set number that is roughly 200 mg/dl in dogs. When blood glucose levels reach this renal threshold, glucose persists in the ultrafiltrate, functioning as an osmotic diuretic and generating polyuria. Compensatory polydipsia and polyphagia are caused by urinary glucose loss, and a lack of insulin-mediated glucose absorption into cells in addition to the emaciation of affected dogs could be due to urine glucose and amino acid loss (American Diabetes Association, 2014). Exocrine pancreatic insufficiency (EPI), which exacerbates weight loss and may first manifest as an increased frequency of feces, may develop in dogs that have pancreatitis as a cause of their diabetes (Bruyette et al., 2020).

DM can lead to cataracts of the eye because the excess glucose in the blood is converted into sorbitol in the lens. This causes a fluid shift in the lens as a result of swelling of the fiber as well as rupture and ultimately cataractogenesis (Wilkie et al. 2006). In cases of hyperglycemia, the kidneys cannot reabsorb all of the glucose, which can pass through the urine, leading to glucosuria. A highly acidic pH is also a common finding in diabetic dogs and is thought to be due to net acid excretion (Choudhary et al., 2021). There is often an increase in the specific gravity of the urine, which is due to the presence of glucose and other solutes (Choudhary et al., 2021). The presence of leukocytes in the urine of a

diabetic dog could be a sign of inflammation or infection in the urinary tract. Diabetic dogs are more prone to urinary tract infections due to the high glucose levels in their urine, which can provide a favorable environment for bacterial growth (Geerlings 2008). Proteinuria may be related to the critical role of glucose in the progression of microvascular damage, resulting in diabetic nephropathy (Abdullaziz et al., 2022).

The decreased levels of RBCs, Hb, and PCV in diabetic dogs could be due to anemia, which is considered a common complication in patients with DM, especially in those with kidney disease. Diabetes may cause kidney vascular damage, which can lead to reduced kidney function and a reduction in erythropoietin (EPO) production, a hormone that stimulates the production of red blood cells in the bone marrow (He *et al.*, 2015). PCV levels in diabetic dogs were decreased as a result of RBC hemolysis (Dallak and Bin-Jaliah 2010). The higher WBCs counts and neutrophils may be associated with the development of retinopathy, albuminuria, and peripheral arterial disease. Previous research has focused on the roles of proinflammatory cytokines in the further development of diabetes complications (Xu *et al.*, 2013). The significant increase in platelets may be due to platelet activation, which is important in atherothrombosis in T2DM, and greater in vivo platelet activation with improved thromboxane production that has been found in patients with impaired glucose metabolism (Santilli et al. 2015).

There was a significant decrease in lymphocyte count in diabetic dogs compared to those in healthy dogs, which may be related to immunodeficiency and high susceptibility to common infectious illnesses associated with DM (Mori et al., 2008). Poorly controlled diabetes can also lead to other complications that affect the immune system, such as neuropathy, retinopathy, and kidney disease (Arya et al., 2011).

Diabetic dogs showed higher RBG than healthy dogs due to inadequate insulin production or insulin resistance (the pancreas is unable to produce enough insulin in type 1 diabetes and the body becomes resistant to insulin in type 2 diabetes), resulting in an increase in blood glucose levels (Bowen et al. 2015). Additionally, we detected a high level of HbA1c in diabetic dogs above 6%, which is regarded as the gold standard for predicting glycemia-related risks for microvascular and macrovascular complications associated with diabetes mellitus over 5–10 years since it indicates long-term blood glucose management (Klein and Buse 2020). Long-term complications of DM may include internal organs such as the liver, so diabetic dogs showed significant elevations of AST and ALT. Our results showed a significant positive correlation ($P<0.05$) between blood glucose levels (RBG and HbA_{1c}) and hepatic function. Diabetic patients have a higher risk of developing fatty liver disease, which is characterized by an increase in fat in the liver. Fatty liver disease is emerging as a major cause of chronic liver disease worldwide, and it is strongly linked to obesity and type 2 diabetes (Leite et al. 2009). Another important organ affected by DM is the kidney. There was a significant increase in BUN, Cr, and symmetric dimethylarginine (SDMA), and our results demonstrated a significant positive correlation ($P<0.05$) between blood glucose level (RBG, HbA_{1c}) and kidney function. Diabetic nephropathy (DN) is a severe complication of diabetes and a main cause of end-stage renal failure, which is the most severe form of kidney disease characterized by a significant decline in kidney function (Zhuo *et al.*, 2013). SDMA is considered a urinary marker for acute renal damage in dogs (Elgazzar et al., 2022).

Because DM could affect the immune status of the affected patient, we measured immunoglobulin to monitor such an alteration. There was a significant decrease in serum immunoglobulin (IgG, IgM, and IgA) in diabetic dogs compared to healthy control dogs because patients with type 1 diabetes were shown to be more susceptible to infections and to have a wide range of humoral and cellular immunological abnormalities (Guo et al., 2016*;* Ahmadiafshar et al., 2015).

As a secondary complication, diabetic patients frequently experience cardiac problems. Troponin T and CK-MB are two unique cardiac markers that we measure. CK-MB and troponin T levels have increased significantly in diabetic dogs and are related to heart muscle damage and myocardial infarction. Our results demonstrated a significant positive correlation ($P<0.05$) between blood glucose levels (RBG, HbA_{1c}) and cardiac damage markers (Troponin T, CK-MB). that hyperglycemia and elevated HbA1c levels are linked to a higher risk of cardiovascular problems such as heart failure and myocardial infarction (Kakey and Hussen 2018).

Regarding ECG changes, there was abnormal T-waves (wide and enlarged) that could be due to diabetes, an established risk indicator for heart disease. Insulin resistance is a precursor and a defining feature of T2DM, and it is also linked to an increased risk of cardiovascular disease, which is attributed to myocardial infarction, a major complication of T2DM (Li-na et al., 2012). Cardiac arrhythmias occur in individuals suffering from type 2 diabetes or prolonged type 1 diabetes who have acquired cardiovascular disease with functional and structural alteration that results in an ischemic substrate for ventricular tachycardia (Andersen et al., 2020).

An ultrasonographic examination of a diabetic dog showed pancreatitis, which may be attributed to irreversible cell death caused by chronic hyperglycemia. Obesity is also an increased risk factor for canine pancreatitis, with increased postprandial levels of triglycerides linked to higher indicators of pancreatic inflammation in obese dogs (Davison, 2015). The liver of a diabetic dog showed fat deposition in the liver. A fatty liver is highly prevalent in patients with type 2 diabetes and obesity. In addition, dyslipidemia, particularly hypertriglyceridemia, is also a well-known predictive factor for the presence of fatty liver disease (Leite et al., 2009). The kidney of a diabetic dog showed nephritis. Because diabetic nephropathy is the most common cause of end-stage renal failure, over time, high blood sugar levels in diabetes can damage the small blood vessels in the kidneys, leading to a gradual loss of kidney function and the development of diabetic nephropathy (Buturovi-Ponikvar et al., 2003). Emphysematous cystitis was observed in some diabetic dogs and could be related to urinary tract infections that may be attributed to high tissue glucose levels, impaired tissue perfusion, and a defective immune response (Fabbi et al. 2016).

5. CONCLUSION

This study revealed long-term complications of diabetes mellitus that affect several organs, such as the eye, liver, kidney, and heart, in chronically diabetic dogs. The preliminary diagnosis of affected cases depended on the changes in clinical manifestation, which were confirmed by hematobiochemical, electrocardiographic, ultrasonographic, and radiographic examination. The chronic cardiac and renal dysfunctions were further confirmed by using specific markers, including troponin T, CK-MB, and SDMA. Accordingly, it is recommended to monitor blood glucose

levels in chronically diabetic dogs to control diabetes and prevent and manage its long-term complications.

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